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# Validation of the 5-Item Medication Adherence Report Scale in Older Stroke Patients in Iran

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**Background:** There is a lack of feasible and validated measures to self-assess medication adherence for older patients with stroke. In addition, the potential determinants of medication adherence for older patients with stroke remain unclear. **Objectives:** The aims of this study were to (1) examine the psychometric properties of a 5-item questionnaire on medication adherence, specifically the 5-item Medication Adherence Report Scale (MARS-5), and (2) explore the determinants of medication adherence. **Methods:** Stroke patients older than 65 years (N = 523) filled out the MARS-5 and the Hospital Anxiety and Depression Scale. The medication possession rate (MPR) was calculated to measure the objective medication adherence. Several clinical characteristics (stroke types, blood pressure, comorbidity, HbA1c, quantity of prescribed drugs, fasting blood glucose, and total cholesterol) and background information were collected. We used Rasch analysis with a differential item functioning test to examine psychometric properties. **Results:** All 5 items in the MARS-5 fit in the same construct (ie, medication adherence), no differential item functioning items were displayed in the MARS-5 across gender, and the MARS-5 total score was strongly correlated with the MPR ($r$ = 0.7). Multiple regression models showed that the MARS-5 and the MPR shared several similar determinants. In addition, the variance of the MARS-5 ($R^2$ = 0.567) was more than that of the MPR ($R^2$ = 0.300). **Conclusions:** The MARS-5 is a feasible and valid self-assessed medication adherence for older patients with stroke. In addition, several determinants were found to be related to medication adherence for older patients with stroke. Healthcare providers may want to take heed of these determinants to improve medication adherence for this population.

**KEY WORDS: adherence, elderly, questionnaire, stroke**

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Stroke is the leading cause of death globally: it is the fifth cause of death in the United States,[1] second in Europe,[2] and sixth in Iran.[3] Stroke often results in functional disability and has a substantial impact on an individual's well-being.[4,5] After a person's first stroke, the cumulative risk of stroke recurrence is 11.1% after 1 year and 26.4% after 5 years.[6] Researchers have identified 1 cause of recurrence to be medication nonadherence, because some studies have shown positive relationships between lower medication adherence and greater incidences of stroke symptoms.[7,8] Guidelines for secondary prevention after stroke have explicitly recommended using appropriate medication to control or reduce both blood pressure and cholesterol level.[9,10] Therefore, promoting medication adherence among stroke patients is critical, and investigating the potential determinants for medication adherence among patients having stroke is important.

Some studies have highlighted the importance of medication adherence in patients with stroke and investigated potential determinants. The determinants include beliefs regarding medications,[11,12] low-density lipoprotein

cholesterol,[13] knowledge about medications,[14] and a patient's emotional state.[15] This is to say that positive beliefs about medications, lower low-density lipoprotein cholesterol, greater knowledge about medications, and less emotional distress are all positively correlated with better medication adherence. Although information about these determinants can help in daily clinical practice, some knowledge gaps exist regarding whether these determinants are applicable to older stoke patients in clinical practice.

To the best of our knowledge, no studies have investigated medication adherence in an older population with stroke. Given the different characteristics (eg, healthy literacy and taking polypharmacy treatment or not) between older and younger stroke patients, the determinants of medication adherence might be somewhat different between the 2 groups. For example, older patients may have poorer health literacy (understanding the importance of each medication and handling adverse effects), a greater need for polypharmacy treatment (older patients are more likely to have comorbidities and need more types of medications than younger patients), and a need to take more doses each day.[16] A review study has identified a variety of potential factors related to medication adherence,[17] and now, empirical studies are needed to conduct a comprehensive assessment of the determinants for medication adherence, including demographics, clinical characteristics, and emotional distress. For example, age and educational level were weakly associated with adherence for older people.[18]

Another practical and important issue is to have a feasible and valid instrument to measure medication adherence for patients with stroke. A potential candidate to assess medication adherence is the Medication Adherence Report Scale (MARS), which has a 10-item version (MARS-10) and a 5-item version (MARS-5). The MARS-10 has been validated for its unidimensionality among people with mental illness;[19,20] however, no studies have examined the psychometric properties of MARS-10 in people with stroke. Similarly, we found that the psychometric evaluation of the MARS-5 has only been done on populations without stroke using classical test theory.[21–23] Although some studies have argued whether the MARS-5 can accurately measure drug adherence,[24,25] other studies have found that the MARS-5 can accurately measure medication adherence.[26,27] In fact, Lin et al[28] concluded that the unique characteristics of different diseases may contribute to different findings regarding the accuracy of the MARS-5. This highlights the importance of conducting a psychometric assessment of the MARS-5 in a specific disease population.

We proposed validating the MARS-5 for use in measuring medication adherence in older patients with stroke. We chose the MARS-5 over the MARS-10 because the MARS-5 is shorter and will therefore have a lower administration burden. Although the psychometric properties of the MARS-5 have yet to be verified in people with stroke, some studies have used the MARS-5 to assess medication adherence in patients with stroke.[11,12] We will adopt modern test theory (eg, the Rasch model) to analyze the psychometric properties of the MARS-5 to fill in the literature gap.

The major benefits of using the Rasch model to test psychometric properties include the following: (1) it estimates the person's ability separately from item difficulty, so the psychometric results are not sample dependent; (2) it produces an ordinal-to-interval conversion table based on the probability that a person responds to a certain answer of an item, and a special unit (ie, logit) is thus generated with the additive characteristics; and (3) it helps to identify which item is an unfair item across subgroups. Differential item functioning (DIF) in the Rasch model can help us to know whether subgroups interpret any item with different considerations.[29] As men and women are very likely to have different thoughts based on different brain structures,[30] testing DIF for MARS-5 across genders is of great interest to healthcare providers. Specifically, we should identify whether the score difference of the MARS-5 reflects the true difference between genders or is due to various interpretations of the MARS-5.[31] Therefore, we claimed that testing DIF across genders for the MARS-5 is a prerequisite before clinical application.

The purposes of this study were to examine the psychometric properties of the MARS-5 in a sample consisting of elderly patients with stroke and to explore the determinants of medication adherence in an older sample with stroke.

## Methods

### Sampling and Setting

The study participants were stroke patients who had been discharged from 5 hospitals in Tehran and Qazvin in 2016. Inclusion criteria were as follows: participants who (1) had a stroke confirmed by neuroimaging, (2) were 65 years or older, (3) were responsible to take their own medication without any help, and (4) had the ability to read and write in Persian, including the ability to provide informed consent to participate in the study. Exclusion criteria were as follows: patients with (1) moderate to severe cognitive impairment (ie, Mini-Mental State Examination score < 18) or (2) dysphasia, aphasia, liver failure, or renal dysfunction. Ethics approval was obtained from the review committees of different universities, and all participants were provided with written informed consent forms.

### Measures

#### Clinical Characteristics

The types of stroke and comorbidity were collected from patients' medical records. Two research assistants

measured blood pressures and drew blood for hemoglobin A1c and lipids. Standard protocol was used to measure systolic and diastolic blood pressure using calibrated mercury sphygmomanometers and appropriately sized cuffs. The level of HbA1c, which indicates the average level of blood glucose levels over 3 months, was obtained from blood samples and assessed using the high-pressure liquid chromatography method. Fasting blood glucose was also assessed using the enzymatic method. Serum lipid (ie, total cholesterol) was directly measured using an esterase/oxidase method. Patients' comorbidity was measured using the Charlson Comorbidity Index.

### Emotional Distress

The Hospital Anxiety and Depression Scale (HADS) was used to collect information on emotional distress, including anxiety and depression performance. The HADS contains 14 items: 7 items measure anxiety and another 7 items measure depression using 4 response categories, where a higher score indicates higher levels of anxiety or depression.[32] The validity of the HADS has been established in patients with stroke.[33] In addition, the Persian version of the HADS for Iranian use has satisfactory psychometric properties, including linguistic validity, internal consistency, known-group validity, construct validity, and unidimensionality for each subscale.[34,35] In the current study, the internal consistency was acceptable for the HADS: $\alpha = .83$ for the anxiety subscale and $\alpha = .89$ for the depression subscale.

### Medication Adherence

The MARS-5 and medication possession rate (MPR) were used to observe the medication adherence of participants. The MARS-5, a self-reported instrument, contains 5 items regarding medication adherence. Each item was rated on a 5-point Likert scale, and the range of the MARS-5 total score is between 5 and 25. A higher score on the MARS-5 represents better medication adherence.[11,36] In addition, the Persian version of the MARS-5 for Iranian use has satisfactory internal consistency.[37] In the current study, the internal consistency was acceptable for MARS-5 ($\alpha = .85$).

The MPR was presented using the number of days of dispensed medications divided by the total number of days. Days of dispensed medications were defined by the number of days on which medications were dispensed to the participants during the study period. The total days were defined by the total number of days in the study period. The calculated values were then multiplied by 100 and presented as percentages. All related information was collected monthly from 13 pharmacies among the 5 hospitals in Tehran and Qazvin and included the total number of pills prescribed along with the dates of each prescription. We assessed cardiovascular, blood pressure–lowering, and diabetes medications adjusted for inpatient days and medication refills before enrollment date, as well as information on prescription changes registered 2 months after discharge.

## Procedure

Patients with stroke were screened at hospitals for eligibility by 3 trained physicians. After confirming eligibility, each participant was asked to sign the informed consent form and then complete the study measures including MARS-5 and HADS 2 months after discharge. The MPR was also calculated 2 months after discharge. Clinical measures were then collected 2 months after discharge to assess the predictive validity of the MARS.

## Data Analysis

Two statistical programs were used for data analysis: DIF and Rasch models used WINSTEPS 3.75.0, and all other analyses used IBM SPSS Statistics 23.0.

Rasch analysis was conducted using a rating scale model to test the item fit and unidimensionality of the MARS-5. The item fit was assessed using 2 mean square (MnSq): the information-weighted fit statistic (infit) and the outlier-sensitive fit statistic (outfit), in which ranges between 0.5 and 1.5 suggest that the item is well fit.[38,39] Unidimensionality was assessed using principal component analysis on the Rasch-retrieved standardized residuals, in which the first component having an eigenvalue of less than 2 indicates unidimensionality.[29] Person separation reliability reported by the Rasch analysis should be less than 0.7 to indicate adequate consistency in the MARS-5.[40] The Likert-type scale of the MARS-5 was examined for its categorical functioning: successive responses for each item score are located in their expected orders. Specifically, the average difficulty of the scores and score thresholds (the thresholds between every 2 scores) should both increase monotonically with the scores.[41] Differential item functioning analysis was conducted to investigate whether male and female stoke patients interpret the MARS-5 differently. A substantial DIF item indicates that the item description has different difficulties for different subgroups of respondents (different genders in this study).[42] We adopted the usual method to identify DIF items: a DIF contrast (ie, the difference of difficulty between 2 groups) of greater than 0.5 suggests a substantial DIF.[43]

We examined the relationship between MARS-5 and the MPR using the Pearson correlation coefficient. Afterward, we constructed 2 regression models to explore the factors for medication adherence measured by the MARS-5 and MPR, respectively. We used a

total score of the MARS-5 and MPR as 2 dependent variables. Demographic variables (age, gender, marital status, monthly family income, and educational level), clinical characteristics (comorbidity, fasting blood glucose test, blood pressure, total cholesterol, and HbA1c), and emotional distress (anxiety and depression) were used as independent variables. All the continuous variables (age, fasting blood glucose test, blood pressure, total cholesterol, HbA1c, and emotional distress) could be viewed as normally distributed. The multicollinearity among the independent variables was acceptable.

Our final sample size (N = 523) was sufficient for all our analyses. The required sample size for Rasch to achieve a stable estimate is 250,[44] especially for a questionnaire using a 5-point Likert-type scale such as the MARS-5. In terms of regression analyses, Austin and Steyerberg[45] suggested that each variable needs 15 to 25 participants. Given that we used 13 variables in each regression model, the sample size fell between 195 and 325.

## Results

Table 1 presents the demographic information, clinical characteristics, emotional distress performance, and medication adherence for the participants (N = 523).

The Rasch analysis showed that the MARS-5 had satisfactory item properties: infit MnSq of 0.74 to 1.25 and outfit MnSq of 0.68 to 1.40. The first eigenvalue of the principal component analysis on the standardized residuals was 1.6, which suggests unidimensionality of the MARS-5. The Person separation reliability of the MARS-5 was adequate (0.74). The categorical functioning of the rating scale in the MARS-5 was within the anticipated monotonic increment: the average difficulties were −6.16 for score 1, −0.28 for score 2, 2.92 for score 3, 4.92 for score 4, and 6.57 for score 5. The score thresholds were monotonically increased: −9.01 from scores 1 to 2, −0.01 from scores 2 to 3, 3.76 from scores 3 to 4, and 5.27 from scores 4 to 5. No substantial DIF items were displayed across genders because all the absolute DIF contrasts were less than 0.5 (see Table 2).

The correlation between the MARS-5 total score and the MPR was strong ($r$ = 0.70, $P$ < .001). In the model with the MARS-5 as a dependent variable, gender, marital status, monthly family income, and all the clinical characteristics were significant predictors. In the MPR model, gender, monthly family income, and all clinical characteristics except comorbidity and HbA1c were significant predictors. Anxiety was significantly associated with the MARS-5 but not with the MPR, whereas depression was significantly associated with the MPR but not with the MARS-5. In addition, female gender, fair to good monthly family income (>$500), and a higher quantity of prescribed drugs were associated with higher MARS-5 and/or MPR scores. Unmarried status; the presence of comorbidities; higher levels of fasting blood glucose, blood pressure, total cholesterol, and HbA1c; anxiety; and depression were associated with lower MARS-5 and/or MPR scores (see Table 3). Because the model using the MARS-5 as a dependent variable had more significant predictors than the model using the MPR as a dependent variable, the former model ($R^2$ = 0.567) explained more variance than did the latter ($R^2$ = 0.300).

**TABLE 1 Participant Characteristics (N = 523)**

| | Mean (SD) or n (%) |
|---|---|
| Demographic information | |
| Age, y | 72.9 (6.5) |
| Gender (male) | 220 (42.1) |
| Marital status (living with a spouse) | 417 (79.7) |
| Educational level | |
| No formal/primary school | 108 (20.7) |
| Primary school | 170 (32.5) |
| Secondary school or higher | 245 (46.8) |
| Monthly family income | |
| Poor ($0–$500) | 189 (36.1) |
| Fair ($500–$1000) | 310 (59.3) |
| Good (>$1000) | 24 (4.6) |
| Clinical characteristics | |
| Diagnosis | |
| Ischemic stroke | 377 (72.1) |
| Transient ischemic stroke | 108 (20.7) |
| Intracerebral hemorrhage | 38 (7.3) |
| Comorbidity (yes) | 256 (48.9) |
| Fasting blood glucose test, mg/dL | 142.92 (67.49) |
| HbA1c | 7.23 (1.32) |
| Systolic blood pressure, mm Hg | 127.26 (14.98) |
| Diastolic blood pressure, mm Hg | 77.46 (9.31) |
| Total cholesterol, mg/dL | 180.53 (78.09) |
| No. prescribed drugs | 3.4 (1.8) |
| Emotional distress[a] | |
| Anxiety | 11.2 (4.1) |
| Depression | 10.1 (4.4) |
| Medication adherence | |
| 5-Item Medication Adherence Report Scale | 21.6 (3.3) |
| Medication possession rate | 61.6 (19.1) |

[a]Measured using the Hospital Anxiety and Depression Scale.

## Discussion

Our psychometric findings demonstrate that the MARS-5 is a valid measure to assess medication adherence in older patients with stroke. Based on the satisfactory results of the Rasch analysis and a high correlation with the MPR ($r$ = 0.7), the MARS-5 may be a useful instrument for clinicians and researchers to measure medication adherence. We extended knowledge about the psychometric properties of the MARS-5 from classic test theory findings to Rasch analysis, including DIF across genders. That is, all the

**TABLE 2 Rasch Analysis on the 5-Item Medication Adherence Report Scale (N = 523)**

| Item No.: Content | Difficulty | Infit MnSq | Outfit MnSq | Difficulty for Men | Difficulty for Women | DIF Contrast |
|---|---|---|---|---|---|---|
| Item 1: change dosage | 0.00 | 0.95 | 0.87 | 0.07 | −0.05 | 0.12 |
| Item 2: forget to take | 1.78 | 1.25 | 1.40 | 2.02 | 1.59 | 0.43 |
| Item 3: stop taking | −1.18 | 1.12 | 1.06 | −1.15 | −1.22 | 0.07 |
| Item 4: skip one of the dosages | 0.05 | 0.87 | 0.83 | −0.22 | 0.24 | −0.46 |
| Item 5: take less than prescribed | −0.65 | 0.74 | 0.68 | −0.81 | −0.54 | −0.27 |

DIF contrast indicates the difficulty for men minus difficulty for women (positive values imply more difficult for men, and negative values imply more difficult for women). Acceptable infit and outfit MnSq is between 0.5 and 1.5; acceptable DIF contrast is less than 0.5.
Abbreviations: DIF, differential item functioning; MnSq, mean square.

MARS-5 items are invariant across genders: male and female patients interpreted the 5 items similarly without substantial DIF, and the items have the same meanings for both genders.

The unidimensionality of the MARS-5 is in agreement with another study on children and their caregivers.[21] Although no studies have used Rasch analysis on the MARS-5, our results are comparable with the findings of 2 recent studies that applied Rasch analysis to the MARS-10 in people with mental illness.[19,20] All of their findings and ours in fit statistics were satisfactory: infit MnSq ranged between 0.74 and 1.25 in our study, between 0.90 and 1.03 in Fond et al,[19] and between 0.92 and 1.03 in Zemmour et al.[20]

There has been a debate as to whether the MARS-5 is an appropriate measure for medication adherence[24–27] and whether different characteristics of disease patients may affect the accuracy of the MARS-5.[28] Based on our rigorous psychometric findings (unidimensionality of the MARS-5, no DIF items in the MARS-5, and a

**TABLE 3 Multiple Linear Regression Models on the 5-Item Medication Adherence Report Scale and Medication Possession Rate (N = 523)**

| | MARS-5 | | | | MPR | | | |
|---|---|---|---|---|---|---|---|---|
| | Coefficient | Standard Error | Standardized Coefficient | *P* | Coefficient | Standard Error | Standardized Coefficient | *P* |
| Demographics | | | | | | | | |
| Age, y | −0.02 | 0.02 | −0.04 | .23 | −0.18 | 0.12 | −0.06 | .16 |
| Female gender (reference: male) | **0.59** | **0.22** | **0.09** | **.01** | **3.39** | **1.60** | **0.09** | **.03** |
| Secondary school or higher (reference: ≤primary) | −0.14 | 0.30 | −0.02 | .64 | 1.22 | 2.23 | 0.03 | .58 |
| Currently unmarried (reference: married) | **−0.88** | **0.34** | **−0.11** | **.01** | −3.80 | 2.49 | −0.08 | .13 |
| Fair and good socioeconomic status (reference: poor) | **0.68** | **0.24** | **0.10** | **.01** | **4.55** | **1.78** | **0.11** | **.01** |
| Clinical characteristics | | | | | | | | |
| No. prescribed drugs | **0.43** | **0.08** | **0.22** | **<.001** | **2.05** | **0.57** | **0.19** | **<.001** |
| Comorbidity | **−0.60** | **0.25** | **−0.09** | **.02** | −1.12 | 1.84 | −0.03 | .55 |
| Fasting blood glucose test, mg/dL | **−0.02** | **0.00** | **−0.48** | **<.001** | **−0.10** | **0.01** | **−0.35** | **<.001** |
| Mean arterial pressure, mm Hg | **−0.08** | **0.01** | **−0.24** | **<.001** | **−0.40** | **0.08** | **−0.22** | **<.001** |
| Total cholesterol, mg/dL | **−0.01** | **0.00** | **−0.16** | **<.001** | **−0.02** | **0.01** | **−0.10** | **.02** |
| HbA1c | **−0.35** | **0.10** | **−0.14** | **<.001** | −0.68 | 0.72 | −0.05 | .34 |
| Emotional distress | | | | | | | | |
| Anxiety[a] | **−0.12** | **0.04** | **−0.15** | **.003** | 0.15 | 0.29 | 0.03 | .60 |
| Depression[a] | −0.04 | 0.04 | −0.05 | .30 | **−0.66** | **0.28** | **−0.15** | **.02** |
| Model statistics | | | | | | | | |
| *F* (*P*) | 46.40 (<.001) | | | | 15.07 (<.001) | | | |
| Degrees of freedom | 13, 460 | | | | 13, 460 | | | |
| $R^2$ (adjusted $R^2$) | 0.567 (0.555) | | | | 0.300 (0.280) | | | |

Significant coefficients are in bold.
Abbreviations: MARS-5, 5-item Medication Adherence Report Scale; MPR, medication possession rate.
[a]Measured using the Hospital Anxiety and Depression Scale.

**What's New and Important**

- The MARS-5 is a feasible self-reported questionnaire to assess medication adherence for Iranian older adults with stroke.
- The MARS-5 shows robust psychometric properties, especially its unidimensionality, in the Iranian older adults with stroke.

high correlation with the MPR), we are confident that the MARS-5 is able to accurately measure medication adherence for older patients with stroke. Nonetheless, future studies are warranted to corroborate with our findings because this is only the first study to investigate the psychometric properties of the MARS-5 on patients with stroke.

Another important issue in psychometric properties for the MARS-5 is the DIF across genders. Different subgroups are likely to interpret item contents differently, especially subgroups that usually have different perspectives, such as the gender subgroups we tested in this study. To fairly assess item scores across subgroups, DIF should be tested before combining or comparing the subgroups' scores.[42] Because no DIF items were displayed, combining or comparing the MARS-5 scores of older male and female stroke patients is acceptable.

Based on the sound psychometric properties, we further investigated possible determinants for medication adherence in older patients with stroke. The associations between demographic variables and medication adherence in our regression model were similar to the findings of 2 review studies: female gender, living with a spouse, and high monthly family income are correlated with increased compliance; age and educational level are weakly associated with adherence, especially for older people.[17,18] In addition, similar to the findings of Phillips et al,[15] our regression model demonstrated that emotional distress was negatively correlated to good medication adherence.

In terms of clinical characteristics, we found that, when the patients had higher scores on the Charlson Comorbidity Index, their medication adherence was poorer. The findings of clinical characteristics are somewhat similar to the study of Cummings et al,[7] in which blood pressure was positively correlated with medication adherence in hypertension patients. Our other clinical characteristics indicated that poor medication adherence existed in stroke patients who had a higher risk of diabetes mellitus. Diabetes mellitus is highly correlated with stroke,[46] and stroke patients are highly likely to have recurrence,[6] so clinicians may want to pay additional attention to these significant clinical characteristics for patients with stroke. Our findings also correspond to the guidelines that suggest controlling blood pressure and cholesterol level.[9,10]

There are some limitations in the study. First, fewer than 10% of our participants were diagnosed with intracerebral hemorrhage, and our results may not be able to generalize to patients with this type of stroke. Second, the study only recruited patients from 5 hospitals in Tehran and Qazvin; thus, the generalizability of our study results might not be applicable throughout Iran. Third, because our sample was Iranian without moderate to severe cognitive impairment, our results are unable to generalize to stroke patients in other countries or those with cognitive impairment. Fourth, our results might be influenced by the different stroke types in our study. Specifically, the pathophysiologic mechanisms between transient ischemic stroke, ischemic stroke, and hemorrhagic stroke are quite different. These different mechanisms might affect the medication adherence of patients with stroke at different levels. Therefore, future studies using a homogeneous sample in stroke type (eg, transient ischemic stroke) and diversity in other populations (eg, Westerners and Asians) are warranted to corroborate our findings. Moreover, future research should consider measuring the functional status of the patients.

## Conclusions

The MARS-5 has satisfactory psychometric properties according to the Rasch model. The results indicate that the scale is unidimensional, the response scale (ie, the 5-point Likert-type scale) functions appropriately, the targeting is acceptable, and no DIF items were displayed across genders. Thus, the MARS-5 might be a useful measure for both clinicians and researchers to assess medication adherence.

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